CLAIMS

1. A method for determining the sequence of a polynucleotide, comprising the steps of:

i. reacting a target polynucleotide with an enzyme that is capable of interacting with and precessing along the polynucleotide, under conditions sufficient to induce enzyme activity; and

ii. detecting conformational changes in the enzyme as the enzyme processes along the polynucleotide.

2. A method according to claim 1, wherein the enzyme is a polymerase enzyme.

3. A method according to claim 1, wherein the enzyme is a helicase enzyme or a primase enzyme.

4. A method according to any preceding claim, wherein the enzyme is immobilised on a solid support.

5. A method according to claim 4, comprising a plurality of enzymes immobilised on the solid support.

6. A method according to any preceding claim, wherein the enzyme comprises a first bound detectable label, the characteristics of which alter as the enzyme undergoes a conformational change.

7. A method according to claim 6, wherein the enzyme comprises a second bound detectable label capable of interacting with the first label, wherein the degree of interaction is dependent on a conformational change in the enzyme.

8. A method according to claim 6, wherein a second detectable label is bound to a nucleotide brought into contact with the enzyme.

9. A method according to claim 7 or claim 8, wherein the first label is an energy acceptor and the second label is an energy donor, or vice versa, and wherein step (ii) is carried out by measuring energy transfer between the two labels.

10. A method according to any preceding claim, wherein step (ii) is carried out using confocal microscopy.

11. A method according to claim 10, wherein step (ii) is

carried out by fluorescence imaging.

12. A method according to claim 6, wherein step (ii) is carried out by measuring a polarisation effect consequent on the altered characteristics of the first label.

13. A method according to claim 12, wherein step (ii) is carried out by fluorescence polarisation anisotrophy.

14. Use of fluorescence resonance energy transfer to detect a conformational change in an enzyme that interacts with and processes along a target polymerase, to thereby determine the sequence of the polynucleotide.

15. Use according to claim 14, wherein the enzyme is a polymerase enzyme.

16. Use according to claim 14 or claim 15, wherein the enzyme is immobilised on a solid support.

17. Use of a detectably-labelled enzyme, capable of interacting with and precessing along a target polynucleotide, to determine the sequence of the polynucleotide, wherein the label alters its detectable characteristics as the enzyme processes along the polynucleotide.

18. A solid support comprising at least one immobilised enzyme capable of interacting with and precessing along a target polynucleotide, the enzyme being labelled with one or more detectable labels.

19. A solid support according to claim 18, wherein the enzyme is a polymerase.

20. A solid support according to claim 18 or claim 19, wherein the label is a fluorophore.

21. A system for determining a sequence of a polynucleotide, comprising a solid support according to any of claims 18 to 21, and an apparatus for detecting the label.